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VARIETIES OF THROMBOPHLEBITIS AND THEIR MANAGEMENT

CLINICAL CLASSIFICATION

Thrombophlebitis may be associated with any one of a variety of pathological conditions.

1. *Recumbency and Quiescence.* Heart failure is more frequently a precipitating cause than is the post-operative or post-partum state. Other causes are fractures, febrile diseases, and paralysis. Predisposing factors are old age, anemia, cancer, sepsis, and varicose veins.

   The process is primary in the deep veins of the legs in the vast majority of cases; the pelvic veins are less often involved. Without anticoagulants or vein ligation pulmonary embolism may be expected in a third of the cases, with death resulting in 4 percent of these cases in all ages, and in even a higher proportion in old age.

2. *Marantic.* This is a terminal form in patients dying of chronic disease. The thrombosis is in the large veins, such as the innominate or the cavae. Pulmonary embolism is almost certain.

3. *Rheumatic.* Aside from recumbency thrombophlebitis, an apparently distinct form may occur in rheumatic fever, in unusual locations such as the neck and upper extremities. Aschoff nodules have been described in the involved vessels. A recurrent migratory form may rarely be seen in rheumatic fever or rheumatoid arthritis, sometimes accompanied by an arteritis.

4. *Carcinogenetic.* Carcinoma predisposes to recumbency and marantic varieties. In addition thrombosis follows extension of the tumor into contiguous veins, as in the pelvis or thorax. Metastases are to be expected from such an extension. A rare effect is an extensive migrating and rapidly recurring form in veins quite removed from the primary or secondary growths. Cancer of the pancreas, stomach, and lungs are most often responsible for this form. Death occurs within months, often from pulmonary embolism. The extensive venous occlusion may cause gangrene.

5. *Blood dyscrasia.* Polycythemia is a common, and leukemia is a rare cause. Chlorosis is said to have been complicated by superior sagittal sinus thrombosis.

6. *Varicose.* Pulmonary embolism is not rare in this common malady, through extension of the thrombus to the deep veins of the calf, or to the femoral vein. This is a special hazard if the patient is confined to bed as for an unrelated operation.

7. *Stasis.* Thrombosis frequently takes place distal to the ligature of a vein. This is particularly true when some thrombosis already exists, as when the saphenous or femoral veins are ligated for thrombophlebitis.

8. *Traumatic and Effort.* Venous thrombosis is a frequent complication about fractures and in a susceptible person may follow even a mild contusion or sprain. Pulmonary embolism is fairly frequent.

9. *Chemical.* The intravenous injection of irritants, such as sclerosing solutions, dextrose, or mercurials, is an adequate cause for thrombosis. The process is usually limited to a few inches of vein. Pulmonary embolism is rare and usually follows propagation of the thrombus during recumbency.

10. *Ischemic.* Thrombosis of the deep veins of a limb may occur in the course of arteriosclerosis and practically always

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occurs after severe arterial thrombosis or embolism. When extensive, this form is very prone to give rise to pulmonary embolism, and it may also precipitate gangrene of the limb. The thrombus may be of the agglutinative type, poor in fibrin, and thus incompletely controlled by anticoagulants.

11. *Thrombo-angiitic.* The deep veins of the lower extremities are regularly involved in Buerger's disease. In addition, forty percent of persons with Buerger's disease suffer a migrating form of thrombophlebitis in the superficial veins of the feet or legs and occasionally of the upper extremities or neck. Pulmonary embolism is infrequent.

12. *Septic.* This is the only form in which bacteria play a demonstrated role. Examples are seen in the portal vein (pylephlebitis) after intraperitoneal sepsis, in the iliac veins after purulent endometritis, and in the internal jugular vein after mastoiditis. Except with pylephlebitis, pulmonary embolism is frequent, and the infarcts may go on to abscess formation.

13. *Idiopathic.* Because we are often unable to demonstrate that any one of the above factors are at work, many thromboses must be consigned to this category. Recurrent and migratory forms are seen. Pulmonary embolism is fairly frequent.

DIAGNOSIS

When the patient has been recumbent, pain in the calf or edema, with or without a rise in temperature, must be accepted as evidence for thrombophlebitis of the deep veins. However, when these symptoms arise while the patient is active, the diagnosis must be approached with some scepticism. Diseases of any of the tissues of the limb have been encountered in patients referred for so-called phlebitis, including arthritis, polyarteritis nodosa, sarcoma of muscle, panniculitis, lymphedema, and several skin disorders—especially the erythemas and pseudoerysipelas complicating dermatophytosis. Biopsy is very helpful and should be used more often. It is important not to mistake the residual symptoms of the post-phlebitic state for new attacks of thrombophlebitis.

Once the diagnosis of thrombophlebitis is made, it is important to determine the nature of the precipitating cause. Conditions of recumbency, trauma, and sepsis should be quite evident. Appropriate examination should likewise lead to the diagnosis of varicose veins, carcinoma, rheumatic disease, ischemia, or blood dyscrasia.

Two forms of migrating thrombophlebitis —that of Buerger's disease and that of occult cancer—may still be culled from the residuum of apparently idiopathic cases. Either form may be suspected when the veins on the dorsum of the feet are involved, since these vessels are not otherwise subject to thrombophlebitis except after local trauma or infection. The patient with Buerger's disease is a smoker, and is less than forty years of age during the initial attack of migrating phlebitis. Lack of peripheral pulses strengthens the diagnosis, but the venous process may precede the arterial. Biopsy of the vein may clinch the diagnosis by revealing the typical intraluminal granuloma. The duration of the thrombophlebitis is of value in the differential diagnosis since death occurs so rapidly in the carcinogenetic form. Moreover, while both varieties are recurrent, the carcinogenetic recurs more rapidly with intervals of only days or weeks between attacks.

The diagnosis of pulmonary embolism must not be lightly made. Sudden chest pain or anxiety, usually with dyspnea, elevation of pulse rate, and fall in blood pressure are early signs. Chills rarely usher in an attack. A pleural friction rub may be heard within several hours or a day, and the pulse and temperature may rise. Bloody sputum and x-ray changes, when present, are noted in a day or two. Myocardial infarction and paroxysmal disorders of heart rhythm are conditions most frequently confused with pulmonary embolism. Early and repeated electrocardiographic examination aids in the differential diagnosis. Rarely pulmonary artery thrombosis may be responsible for infarction, the diagnosis depending on other clinical circumstances.

TREATMENT OF RECUMBENCY THROMBOPHLEBITIS

1. *Prophylaxis.* The more normally the patient can be maintained, the less likely is he to develop thrombophlebitis. This means adequate correction of anemia, dehydration, and sepsis. Varicose veins should be operated on several weeks in advance of other anticipated operations; otherwise treatment of the varices should be postponed to avoid the consequences of the stasis thrombosis that follows surgery on the varices. Early exercise and ambulation has not lowered the incidence of thrombophlebitis but has reduced the number of fatal emboli. The same may be said of the wearing of elastic bandages or stockings during recumbency. Anticoagulants and vein ligation have both been used prophylactically, but this seems necessary only in those who have suffered thrombophlebitis or pulmonary embolism during previous confinement to bed.

2. *Measures to prevent pulmonary embolism.* These must be instituted immediately. Anticoagulant therapy is the usual method of choice. *Heparin* is the preferred drug, because of its rapid action, tolerance to a wide range of dosage, easy reversibility of action, and its apparent ability to inhibit some thromboses resistant to dicumarol. We give sodium heparin subcutaneously every 6 to 12 hours in a dose (average 60 mg.) adequate to raise the coagulation time to 30 to 45 minutes, in blood drawn at the peak of effect about 2 hours after giving a dose. The drug may be given intermittently in a vein in somewhat smaller doses. If the daily test shows too prolonged a coagulation time, the next dose should be omitted and subsequent doses made smaller. A course of treatment should last 7 to 10 days, the heparin being given every 12 hours after symptoms have begun to subside. Precipitation of new thrombosis has followed sudden cessation of treatment even when dicumarol has been given at the same time. The dosage of heparin should therefore be gradually reduced during the last 36 hours. If, for example, 60 mg. sodium heparin has been required at each dose, the last 3 doses might consist of 30, 30, and 20 mg. respectively. Depository forms of heparin may be used for prolonging the treatment at home. 200 mg. of such a preparation (Depoheparin (R)) may be given every day or every other day, depending on the sensitivity demonstrated by the patient to the ordinary heparin previously given.

Vein ligation is preferable to anticoagulant therapy under the following conditions: (1) the state responsible for the thrombophlebitis is expected to endure or recur. Examples are a continuing tendency to heart failure, the need for further major surgery, or the presence of hemiplegia or debility. (2) Anticoagulants are contraindicated because of a bleeding tendency, as in bleeding peptic ulcer or esophageal varices, or because of the nature of an operation, such as prostatic resection or procedures on the central nervous system. (3) Pulmonary embolism has occurred. In the last instance, ligation of the common femoral veins should be done if the ligation will lie proximal to the thrombus; otherwise anticoagulants may be tried, reserving ligation of the inferior vena cava if still another embolus occurs. Ligation at whatever level is necessary should be done without delay if one or more emboli have followed adequate anticoagulant treatment. (4) Pulmonary embolism has occurred during some previous illness.

Ligation of the femoral vein must be done above the entrance of the deep femoral vein, since emboli, during the current or later attacks, may come from the deep vessel. As a rule, the operation will not give rise to much distal edema if the ligature is placed below the circumflex femoral veins and if heparin is given postoperatively to limit the stasis thrombosis. Heparin should also be used after ligation of the vena cava. Thrombectomy is not indicated as an elective procedure, but a lightly adherent thrombus may be removed if gentle suction will extract it.

Ligation of the femoral veins after a non-fatal embolus is of questionable use if there have been no localizing signs of thrombophlebitis in the lower extremities. The operation should also be avoided in the ischemic limb because it increases the tendency to gangrene.

3. *Treatment of pulmonary embolism.* It is essential to administer oxygen in this emergency. Some sedative is usually necessary, and intravenous papaverine in a dose of 30 mg. is often used on the basis that it relaxes spasm of the pulmonary artery. Its effect is uncertain, and some patients have succumbed to its rapid injection. Unless there is a contraindication sodium heparin in an average dose of 60 mg. should be given intravenously to diminish propagation of the thrombus in the lung and for its effect on the thrombophlebitis. If vein ligation is contemplated, heparin should be withheld for at least 4 hours prior to the operation. If necessary the effect of heparin may be abolished in about an hour by the intravenous injection of 50 mg. of protamine sulphate. Penicillin or some other antibiotic should be given because infection occasionally develops in the infarct or in the pleural exudate. If large in amount, the fluid should be removed because it is apt to be bloody and fibrogenic.

4. *Treatment of the local process.* While the thrombophlebitis is active, the patient should be in bed, with his legs elevated and bandaged snugly with elastic bandages. Motion and exercise should be encouraged since inactivity leads to propagation of the thrombus and increases the danger of embolism. Ice caps should not be used since they increase vasospasm and probably promote thrombosis. Except in purulent thrombophlebitis antibiotics do no good and should not be used. Anticoagulants are very important since, by diminishing the extent of thrombosis and hastening its resolution, less damage is done to the veins and their valves. Sympathetic nerve block is helpful if pain

and vasospasm persist. If anticoagulants are being used, they must be interrupted temporarily, otherwise the needle puncture may cause serious hemorrhage. During recovery, elastic bandages or stockings must be continued for at least as long as there is evidence of edema. This is important to diminish post-phlebitic changes.

MODIFICATION OF TREATMENT IN OTHER VARIETIES

The treatment outlined for recumbency thrombophlebitis is generally applicable to other forms. However, the following exceptions may be noted. Pulmonary embolism is not to be expected from thrombophlebitis of the upper extremities, save in the marantic form, and ligation of these veins therefore need not be done. The same is true of thrombosis of the superficial veins of the lower limbs except in varicose veins. In general, patients with involvement of the superficial veins of the lower limbs should be treated with elastic compression and continued activity since rest in bed favors propagation to the deep veins.

Thrombophlebitis of varicose veins is successfully treated during the stage of activity by saphenous vein division plus division of communicating veins when indicated. Heparin should be given for a few days postoperatively to older patients, who may develop deep thrombosis and pulmonary embolism. Elastic support with continued activity is proper if operation must be postponed for a few days.

Ischemic thrombophlebitis is treated by heparin, with as much activity as the ischemia will allow, and by measures to increase the blood supply if feasible. Here sympathectomy is occasionally helpful.

Cessation of smoking is basic in the treatment of phlebitis associated with Buerger's disease. Resolution of the process may require some weeks. Sympathectomy is indicated if there is significant arterial occlusion; it will hasten resolution of the venous process. Intravenous typhoid vaccine or subcutaneous sterile milk injection are also helpful. A similar and surer effect may be obtained through the use of ACTH subcutaneously, using 40 mg. daily in a gelatin menstruum. Oral cortisone may be preferred in a dose of 200 mg. daily. Inadequate treatment may be followed by a flare-up. ACTH therapy added to heparinization is occasionally helpful in the migrating thrombophlebitis of visceral carcinoma where gangrene seems imminent.

Septic thrombophlebitis is usuall controlled by intense antibiotic therapy, but ligation of the vein may be necessary to halt septicemia and septic emboli. Rarely, pus filled veins must be drained or excised.

Idiopathic thrombophlebitis usually reacts well to anticoagulants although ligation is sometimes required when an attack involves the deep veins of the leg and gives rise to pulmonary embolism. There is no effective way to prevent recurrence of attacks. The writer has observed no benefit from cessation of smoking in this group.

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ANNUAL MEETING AND SCIENTIFIC SESSIONS

The Twenty-Ninth Annual Meeting and the Twenty-Sixth Scientific Sessions of the American Heart Association will be held at the *Hotel Chelsea* in Atlantic City, N. J., *April 8-12, 1953*, immediately preceding the annual meeting of the American College of Physicians. All those desiring to attend should make room reservations at the earliest possible date. (The Hotel Chelsea is located on the Boardwalk at Morris Avenue, 5 short blocks *south* of the Convention Hall.) The Scientific Sessions will be held on Thursday, Friday, Saturday and Sunday, April 9, 10, 11 and 12.

PAPERS FOR THE SCIENTIFIC SESSIONS

All those desiring to present papers at the Association's Scientific Sessions should submit abstracts *in triplicate* of the proposed presentation to Dr. André Cournand, Chairman of the Program Committee, c/o American Heart Association, 44 East 23rd Street, New York 10, N. Y., not later than *January 1, 1953*. Abstracts should not be longer than 300 words and must contain in summary form, a specific statement of the results obtained or conclusions reached (not merely a statement that results or conclusions will be presented, or discussed at the meeting.)